

GASTRIC EMPTYING IN INFANCY

Influence of meal composition and some
clinical conditions

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Lund 1981

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- I. Cavell B. Gastric emptying in preterm infants. Acta Paediatr Scand 1979; 68:725-730.
- II. Cavell B. Gastric emptying in infants fed human milk or infant formula. Acta Paediatr Scand 1981; in press.
- III. Cavell B. Gastric emptying in infants with congenital heart disease. Acta Paediatr Scand 1981; in press.
- IV. Cavell B. Effect of feeding an infant formula with high energy density on gastric emptying in infants with congenital heart disease. Acta Paediatr Scand 1981; in press.
- V. Cavell B. Gastric emptying in infants with cystic fibrosis. Acta Paediatr Scand 1981; in press.



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ABBREVIATIONS

AGA	= appropriate for gestational age
CA	= coarctation of the aorta
CF	= cystic fibrosis
CHD	= congenital heart disease
CHF	= congestive heart failure
CPAP	= continuous positive airway pressure
ET	= exchange transfusion
EF	= endocardial fibroelastosis
FG	= failure to grow
IPPV	= intermittent positive pressure ventilation
IRDS	= idiopathic respiratory distress syndrome
PDA	= patent ductus arteriosus
PEG	= polyethylene glycol
PH	= pulmonary hypertension
RIS	= respiratory insufficiency syndrome
TGA	= transposition of the great arteries
TT	= transient tachypnoea
VSD	= ventricular septal defect

INTRODUCTION

Although knowledge of the reservoir and emptying function of the infant's stomach seems important in many clinical conditions, there is a scarcity of quantitative information in this field. This scarcity, and the disagreements within the existing literature, can be attributed to the slow development of suitable techniques for measuring gastric emptying of a meal.

Methods of study

Radiological techniques for studying gastric emptying in infants and children were already in use in the early twentieth century (26) and these techniques were the ones most commonly used in studies on gastric emptying in infants until recently. Emptying was estimated in terms of gastric emptying time, i.e. the time taken for the stomach to empty a specified fraction of its contents (6,30). Difficulties in assessing gastric emptying quantitatively and variations in technique seem to have been major obstacles to getting consistent data with radiological techniques. Thus, gastric emptying times ranging from 1 1/2 to 24 hours are reported in the newborn infant (33). In addition radiation hazards made these methods less suitable for studies in infancy, and they have largely fallen from use.

Using a radioisotope, indium-113 microcolloid mixed with a meal and detected by a gamma camera Signer and Fridrich (32) studied gastric emptying in healthy neonates and infants with pyloric stenosis. They found that gastric emptying generally followed an exponential

pattern. Gastric half-emptying times, i.e. the time taken for the stomach to empty by half, varied considerably. A similar technique involving the use of technetium-99 was applied in a study of gastric emptying of a solid meal in infants (1). These methods assume a constant relationship between the measured radiation and the quantity of radionuclide in the stomach, a condition which may not be fulfilled because of changes in distance between source and detector, i.e. a "geometrical error" (13). Furthermore, superposition of parts of the stomach and some part of the small intestine makes separation of emptied and retained meal difficult.

Vendel (34) measured gastric emptying of milk meals in infants aged 1 week - 11 months using naso-gastric intubation. At regular intervals after administration of the meal the gastric contents were aspirated, the volume recorded, and reinserted into the stomach. In most infants he found a rectilinear emptying pattern during almost the whole meal, but he reported no quantitative data.

Keller (25) used a similar technique in studying gastric emptying in infants. One hour after administration of the meal the gastric contents were aspirated and measured. However, when reinserting the aspirated gastric contents he added a new meal volume to replace the volume that appeared to have left the stomach. The procedure was repeated several times and the average of the added meal volumes was used as a measure of gastric emptying rate. This figure proved to be strongly correlated with the infant's body surface area. Keller's

technique gave no information of the gastric evacuation of a single meal.

The introduction of dilution markers suitable for use in the stomach yielded more accurate information on gastric emptying in infants. The most commonly used markers have been phenol red and polyethylene glycol, which have both proved reliable as gastric markers in man (25). Phenol red binds to protein which precludes its use in meals containing protein.

Husband and Husband (21) studied gastric emptying of water and glucose meals in the newborn using the Serial Test Meal (18). The technique involves repeated nasogastric intubations on consecutive days at varying intervals after administration of a test meal containing phenol red. By aspirating and washing out the gastric contents the amount of meal remaining in the stomach can be calculated. By putting together the results from various days information on the gastric emptying pattern and gastric emptying rate can be obtained. Husband and Husband found that the higher the concentration of glucose in the meal the slower the gastric emptying (vide infra). The Serial Test Meal does not allow one to follow the emptying of a single meal. This is a disadvantage when a study concerns the influence on gastric emptying of clinical conditions which may change within the course of days or weeks.

Other investigations used a simplified version of the Serial Test Meal by measuring gastric retention of a glucose meal at 30 minutes after its administration (2, 4, 16, 35). This technique is useful for comparing groups of infants but does not give the complete pattern of

emptying of a single meal. Yu (35) reported on the effect of body position in the neonate and found that the stomach emptied faster in the prone and right lateral positions than in the supine and left lateral positions. Gupta and Brans (16) in a study on gastric emptying in healthy neonates during the first 60 hours of life reported that 30-minute gastric retention was affected by gestational maturity. Blumenthal (2,4) found no effect of temperature of the meal, phototherapy or metoclopramide on gastric emptying in the newborn.

George (15) described a method for studying gastric emptying of a single fluid test meal containing phenol red as a marker. The method which involves naso-gastric intubation and a double-sampling dye-dilution technique makes it possible to follow the gastric evacuation of a single meal during the whole postprandial period. I modified the method for use in infants given meals of human milk or infant formula using PEG instead of phenol red as a marker (9,11). Blumenthal et al. (3) using a similar technique found no postural differences in the pattern of stomach emptying of glucose meals in the newborn. The method has also been used in studies in gastric emptying in children (14) and preterm infants (31).

Regulation of gastric emptying

The stomach receives food, stores it and regulates its delivery into the duodenum. The proximal area of the stomach has a reservoir function, which involves receptive relaxation of the stomach wall allowing the fundus to accomodate increased volume without increasing

intra-gastric pressure (8). The distal area of the stomach is involved in the emptying of solid food but it also plays a part in the emptying of liquids.

Gastric emptying of fluids depends on the size of the pyloric opening and on the difference between intra-gastric and intraduodenal pressure. Distension of the stomach is the only natural stimulus known to increase gastric emptying (19). High osmolality, fat and acid in the duodenum slow gastric emptying (19). Thus, the volume as well as the composition of a meal are important. The consistency of a meal also influences the emptying rate, fluids leaving the stomach faster than solids (12). Fat is a powerful inhibitor. Triglycerides require digestion in order to slow gastric emptying. Liberated fatty acids are supposed to act on receptors in the proximal small intestine (19). The higher the osmolality of a meal the slower the stomach empties. Consequently, osmoreceptors in the duodenum located deep to the brush borders of the enterocytes have been postulated to participate in a negative feed-back mechanism (19). Inhibition of gastric emptying by the products of protein digestion (7) is probably mediated by the same osmoreceptors as those responding to amino acids (12) and carbohydrates. Hunt and Stubbs recognized a slowing of gastric emptying with increasing energy density of meals (20).

There are very few studies dealing with the physiological aspects of regulation of gastric emptying in infants. Husband and Husband (21) concluded that osmoreceptors responsive to glucose were functional in the first few days of life. In a study on the early gastric emptying phase in infants I found that it was influenced

by meal volume and by osmolality dependent inhibitory mechanisms operating within the first few minutes after feeding. Thus gastric emptying was slowed to far below the potential rate (10).

The aim of the investigation

The aim of the present work was to study gastric emptying in infants in some clinical situations where alterations in gastric function could be expected. Furthermore, the influence of meal composition was considered to be important.

METHODS

Measurement of gastric emptying

The essentials of the procedure and the technique for estimating gastric emptying in infants, which are presented in detail in paper I, are as follows.

A test meal containing polyethylene glycol (PEG, Macrogol 3000) in a concentration of 0.1 to 0.25 % (w/v) is given by naso-gastric tube. At various intervals after administration of the meal the amount of meal remaining in the stomach is estimated by injecting into the stomach a known amount of an aliquot of the meal containing PEG in a higher concentration (1.5 to 4 %). The aliquot is mixed with the gastric contents by withdrawing and re-instilling with a syringe for 2 to 3 minutes. Before and after adding the aliquot, samples are withdrawn from the stomach for estimation of PEG concentration. The volume of the gastric contents is

calculated from an equation for marker dilution (I) and the amount of meal remaining is obtained from the volume of the gastric contents by correcting for the calculated dilution with secretions. The procedure is finished by withdrawing and washing-out the remaining gastric contents 50 to 160 minutes after administration of the meal.

Durations were chosen considering the expected rate of gastric emptying of the infant. Thus, studies in pre-term infants and in infants with CF generally lasted 1 to 1 1/2 hour, while studies in healthy infants and in infants with CHD lasted about 2 hours.

Individual emptying curves were plotted and used for estimating gastric half-emptying time and emptying rate. The latter was expressed as amount of meal (ml) emptied per 0.1 m^2 of body surface area per hour.

The use of a marker dilution method assumes that the marker is distributed evenly in the gastric contents. The marker should be non-toxic and it should not influence on gastric emptying. PEG has been validated as a non-absorbable water-soluble marker for the quantitative study of human gastric function (23) and it has been used in studies of gastric emptying in man (24,27).

Ideally, complete mixing of the marked added to the gastric contents should be achieved within a brief period during which no significant change of the volume of the gastric contents occurs, i.e. within a few minutes. PEG in the concentrations used in the present study is quickly dissolved after injection in the

gastric contents, as evidenced by the rapid and complete increase of its concentration.

Proper positioning of the tube in the infant's stomach is essential. If the opening of the tube is positioned too close to the pylorus, injected PEG solution may leave the stomach before mixing with the gastric contents, resulting in a spuriously large volume reading. Furthermore, vigorous aspiration and reinstallation with the syringe may cause regurgitation from the duodenum.

With the chosen span of PEG concentrations the precision in measuring concentration differences of the marker, and thus the volume of gastric contents, restrict the number of volume determinations that can be performed during a study. The error in estimating the amount of meal remaining in the stomach depends on the errors and the size of the variables of the equation for marker dilution (I). For practical reasons only the assay of marker concentration matters, as the amount of marker added is weighed accurately. The error in measuring PEG as shown by double determinations, is 0.10 mg/ml in the concentration interval 2 to 7.5 mg/ml. Above this interval the error is 0.15 mg/ml. By adding the marker in an amount roughly adapted to the expected amount of meal remaining in the stomach and its marker concentration, a suitable increase in PEG concentration can be achieved, giving a tolerable percentage error in estimation of meal volume.

In the present studies generally 2 to 4 volume determinations were performed. The increase of the concentration of PEG at the volume determinations usually varied

between 2.5 to 6 mg/ml. The resulting percentage error in meal volume was in the order of 5 to 15 %. The precision of the method is evidenced by a model experiment (I).

Statistical methods

Standard statistical methods were used in the statistical analysis. The level of significance was chosen at 5 %.

Analytical method

PEG was estimated by the method of Hydén (22) using the modifications by Boulter and McMichael (5).

Body surface area was calculated using a height-weight formula (17).

CLINICAL MATERIAL

The clinical material consists of 40 infants aged 1 week to 6 months. Twenty-eight infants were admitted to the Department of Paediatrics, Lund, and 12 were attending Baby Health Care Centres in Lund. The distribution of the clinical material is shown in Table 1. Individual data on age, weight and body surface area are presented in Tables 1 to 4 in the Appendix. Individual data on gestational age in preterms are presented in Table 1 of paper I.

The series of healthy infants comprised 12 infants attending Baby Health Care Centres in Lund and 5 admitted to the Department of Paediatrics, Lund. All the infants were born at term. The five infants who were in hospital were admitted for investigation of symptoms which were considered of no importance for gastric function or had disappeared at the time of the study.

The series of 8 infants with CHD included one patient with cyanotic heart disease. Six of the patients with CHD were in heart failure. All the patients with CF had pancreatic insufficiency.

Table 1. Clinical material

	n	Gest.age (weeks)	Age (weeks)	Weight (kg)	Paper
Preterms (AGA)	11	28-34	1-9 ¹⁾	1.075-1.900	I
Healthy infants	17		4-24	3.45 -7.29	II,III,V
Infants with CHD	8		1-22	3.30 -5.88	III,IV
Infants with CF	4		7-19	3.50 -5.10	V

1) Corresponding to a gestational age of 33 to 38 weeks.

A total of 76 studies were performed in the 40 infants.

RESULTS

GASTRIC EMPTYING IN PRETERM INFANTS (I)

Knowledge of the gastric emptying and reservoir functions of the preterm infant seems important, considering the nutritional problems peculiar to this group of in-

fants. Gastric emptying was therefore studied in 11 healthy preterm (AGA) infants weighing 1 075 to 1 900 g at a postnatal age of 1 to 9 weeks. A total of 30 studies, including 22 with meals of human milk and 8 with infant formula, were performed.

Results. Gastric emptying of human milk generally followed a biphasic pattern with an initial rapid phase followed by a slower phase. The emptying of meals of infant formula usually followed a linear pattern. Gastric half-emptying times were 25 and 51 minutes with meals of human milk and infant formula, respectively, the difference being significant. After 51 and 80 minutes three quarters of the meals of human milk and infant formula, respectively, had left the stomach. Gastric emptying rate was 19.4 ± 4.5 and 13.8 ± 2.8 ml/ 0.1 m^2 of body surface area/hour with meals of human milk and infant formula, respectively. The difference is significant. Gastric emptying rate was related to the infant's body surface area and body weight. It was not significantly correlated to postconceptional age.

GASTRIC EMPTYING IN INFANTS FED HUMAN MILK OR INFANT FORMULA (II)

The nature of a test meal was found to influence gastric emptying in healthy preterm infants (I). The second study was designed to investigate if the same influence was discernable in healthy infants born at term. Seventeen healthy infants aged 4 weeks to 6 months were studied. A total of 24 studies including 15 with meals of human milk and 9 with infant formula, were performed.

Results. Again, gastric emptying of human milk generally followed a biphasic pattern with an initial rapid phase followed by a slower phase. As in preterm infants meals of infant formula were emptied in a linear fashion. Gastric half-emptying times were 48 and 78 minutes with meals of human milk and infant formula, respectively, the difference being significant. Gastric emptying rate was 29.5 ± 4.6 and 22.7 ± 4.2 ml/0.1 m² of body surface area/hour for meals of human milk and infant formula, respectively. The difference is significant. During the second hour of the study gastric emptying rate was, however, equal with the two meals.

GASTRIC EMPTYING IN INFANTS WITH CONGENITAL HEART DISEASE (III)

Alterations in gastric emptying function could contribute to the poor intake of food commonly seen in the infant with CHD. The aim of this study was to estimate gastric emptying in infants with severe CHD. Eight infants with CHD aged one week to 5 months were studied. Six of them were in heart failure and seven of them, being unable to consume sufficient food volumes, were fed through a feeding tube. A group of 9 healthy infants aged 4 weeks to 6 months were used as controls. All the infants were given meals of infant formula. Meal volumes were 23 and 33 ml per kg for CHD and normal infants, respectively.

Results. Gastric emptying pattern was linear in 5 and biphasic in 2 infants with CHD. Both after one and two hours significantly smaller amounts of meal had emptied from the stomach in the infants with CHD as compared

with the controls. The emptying rate during the second hour of the study was equal in the two groups.

EFFECT OF FEEDING AN INFANT FORMULA WITH HIGH ENERGY DENSITY ON GASTRIC EMPTYING IN INFANTS WITH CONGENITAL HEART DISEASE (IV)

The feeding of small volumes of formula with a high energy density has been suggested in order to provide an adequate nutritional supply to infants with CHD. The purpose of this study was to assess the influence of raising the energy density of a meal on gastric emptying in infants with severe CHD.

Seven infants, who took part in a previous study (III), received an extra meal of infant formula fortified with a glucose polymer (Caloreen). Gastric emptying of the fortified meal was compared with the emptying of the meal of standard infant formula.

Results. Gastric emptying pattern was not changed appreciably by adding Caloreen to the meals. Gastric half-emptying times were, however, prolonged significantly. After 2 hours a slightly but significantly smaller amount of meal containing Caloreen than standard infant formula had emptied from the stomach. Nevertheless, the net transfer of energy to the intestine was larger than after feeding a meal of standard infant formula.

GASTRIC EMPTYING IN INFANTS WITH CYSTIC FIBROSIS (V)

Rapid gastric emptying caused by inefficient feedback inhibition of the stomach due to inadequate digestion

of food has been reported in patients with pancreatic insufficiency. Exocrine pancreatic insufficiency is present in early life in a majority of patients with CF. Gastric emptying was therefore assessed during the first few months of life in infants with CF.

Four infants aged 5 weeks to 4 months all of them having pancreatic insufficiency were studied. They received meals of pasteurized human milk or infant formula.

Results. Three patients had higher gastric emptying rates during the first hour than the controls. In one of the patients who was given meals both of human milk and infant formula, gastric emptying was not influenced by the type of the meal, the meals emptying at a similar rate.

CONCLUSIONS AND DISCUSSION

Gastric emptying was clearly influenced by the quality of the meal. This was obvious both in preterm and term infants and hence the difference in gastric emptying is not related to the maturity of the infant. Gastric emptying usually followed a biphasic pattern with meals of human milk, while the emptying of infant formula was linear. Emptying with an initial rapid phase contributed to the shorter half-emptying times and higher emptying rates during the first hour with meals of human milk.

A biphasic emptying pattern with an initial rapid phase lasting about 5 minutes, followed by a linear phase, has been found in adults given composite test meals (29). The initial phase was believed to be influenced mainly by osmoreceptors and the second by receptors responding to fat. It is not possible to discern an initial phase of such short duration with the technique used in the present study, and therefore the influence of a meal on a particular phase cannot be attributed to any particular component or quality of the meal.

As the two meals do not differ in osmolality or carbohydrate content, the explanation for the difference in emptying may be found in their fat and protein components. Although they differ only slightly in their concentration of individual fatty acids, differences in digestion of fat may contribute to the varying behaviour of the two meals. A slower emptying of infant formula can then be explained if the formula fat could prove to be digested faster than human milk fat.

The difference in protein concentration is probably too small to explain the varying emptying of the two meals. Slower emptying due to differences in protein digestibility would suggest infant formula protein to be hydrolysed faster than human milk protein, a possibility that must be investigated further.

Adding a glucose polymer to the meal of the CHD infants slowed gastric emptying slightly during the second hour of the study. This is consistent with a submaximal inhibition by the standard meal. The larger net transfer of energy to the intestine with meals with raised

energy density seems to be an advantage obtained without disturbance of gastric emptying, e.g. gastric retention.

Gastric emptying was related to body size both in pre-term and term infants. Preterm infants had slower gastric emptying rates than term infants, when compared on a body surface area basis. Since their meal volumes were small, their half-emptying times were rather short.

The infants with CHD showed slower gastric emptying during the first hour. This may also be a consequence of their small meal volumes. However, considering that their emptying rate was not much greater than that of preterm infants receiving even smaller meals, other factors, e.g. the clinical condition of the infant, may have influenced on gastric emptying. Gastric emptying of the CHD and normal infants was equal during the second hour of the study. At this stage it seems that the emptying rate is more dependent on inhibition from the small intestine than on the volume of the gastric contents.

The rapid gastric emptying which was observed in three of the patients with CF can be explained by assuming maldigestion of the meal in the duodenum causing inadequate inhibition of the stomach. In patients with pancreatic insufficiency, the lack of ability to delay gastric emptying of a meal is probably related to their decreased ability to absorb fat (28). This is consistent with the finding of a normal gastric emptying rate in one patient with CF who had some pancreatic enzyme secretion, compared to the three patients with rapid gastric emptying who had virtually no pancreatic enzyme activity left.

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APPENDIX

GASTRIC EMPTYING IN PRETERM INFANTS

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ABSTRACT. Cavell, B. (Department of Paediatrics, University of Lund, Lund, Sweden). Gastric emptying in preterm infants. *Acta Paediatr Scand*, 68: 725, 1979.—The gastric emptying of meals of human milk and infant formula was studied in 11 healthy preterm (AGA) infants at a postnatal age of 1-9 weeks corresponding to 33-38 weeks of gestational age. A total of 30 studies were performed using a marker dilution technique. Gastric emptying of meals of human milk followed a biphasic emptying pattern with an initial fast phase. In about 25 min half of the meal had left the stomach. The emptying of meals of adapted infant formula usually followed a linear pattern and half the meal had left the stomach after 51 min. After one hour an average of 24.8 ml of human milk and 19.2 ml of infant formula had left the stomach.

KEY WORDS: Gastric emptying, preterm infants

In recent years there has been a growing interest in the feeding of the preterm infant. Various techniques in providing these infants with an adequate nutritional supply, e.g. nasogastric and transpyloric feeding, have been suggested. There are, however, reports on intestinal complications in preterm infants receiving transpyloric feedings (4, 8, 14). Nasogastric feeding is not associated with such complications. This technique carries, however, the risk of regurgitation and aspiration of gastric contents when the volume of the meal exceeds the capacity of the infant's stomach for handling it. On the other hand, too small meal volumes may not fulfill the nutritional demands of the infant. Knowledge of the reservoir function of the stomach of the preterm infant would thus seem important. The purpose of the present study was to estimate quantitatively the gastric emptying function in healthy preterm infants fed complete meals.

MATERIAL

Eleven preterm infants were studied at a postnatal age of one to nine weeks. The clinical data on the infants are presented in Table 1. Gestational age was calculated

from the first day of the mother's last menstrual period. The degree of maturity was furthermore estimated by assessing external features, neurological development and head circumference (5). Body surface was estimated according to Haycock et al. (7). All infants were appropriate in weight for gestational age (AGA) according to Swedish standards (18). At the time of the studies all the infants were healthy and growing normally. They were nursed in incubators and fed through a nasogastric infant feeding tube. The studies were made after informed consent of the mothers.

METHODS

General procedure. Each infant was studied on one to five occasions making a total of 30 studies in the eleven infants. The infants were given luke-warm test meals of fresh frozen human milk usually obtained from their own mother or an adapted infant formula. The composition of the infant formula used is shown in Table 2. The volume of the test meal was about 22 ml/kg body weight corresponding to the volume of the infant's ordinary meal.

Part of this work was presented at The Joint Meeting of the European Society for Pediatric Gastroenterology and Nutrition & The North American Society for Pediatric Gastroenterology in Paris, May 4-6, 1978 (3).

Abbreviations: IRDS = idiopathic respiratory distress syndrome; RIS = respiratory insufficiency syndrome (15); TT = transient tachypnoea; IPPV = intermittent positive pressure ventilation; CPAP = continuous positive airway pressure; ET = exchange transfusion.

Table 1. Clinical data in preterm infants

For abbreviations, see text

Patient no.	Sex	Birth weight (g)	Gestational age at birth (weeks)	Previous history
1	f	950	29	Chylothorax. IPPV 7 days, CPAP 2 days
2	f	1 800	32	Twin, TT
3	f	1 815	32	Twin
4	m	1 940	34	
5	f	960	29	RIS. IPPV 9 days, CPAP 2 weeks
6	f	910	28	IRDS. IPPV 19 days, CPAP 4 days
7	f	1 020	31	
8	m	900	28	IRDS. RIS. IPPV 6 weeks, CPAP 3 hours
9	f	1 555	32	TT
10	f	1 280	32	Twin, IRDS. IPPV 1 day, CPAP 4 days.
				Hyperbilirubinemia. ET
11	f	1 350	32	Twin, IRDS. CPAP 5 days

A French size 5 infant feeding tube was introduced into the stomach through the nose. The gastric contents were withdrawn and the stomach was washed out with saline immediately before the test meal was injected. During the study the infant was lying prone or in the right lateral position in an incubator.

Amount of test meal in the stomach. The amounts of test meal remaining in the stomach after various intervals were estimated using a modification of an earlier described procedure (2). A marker dilution technique is used after the infant has received a test meal containing polyethylene glycol (PEG, Macrogol 3000). To an aliquot of the test meal is added a specified amount of PEG. This aliquot is introduced into the stomach and mixed with the gastric contents by withdrawing and reinserting with a syringe for 2 min. Immediately before and after this procedure samples are withdrawn from the stomach for the estimation of PEG concentration.

The first volume determination was thus performed 10–20 min after feeding had started. The procedure was

repeated once or twice at various intervals during one study.

The volume of the gastric contents, V , is calculated from the equation:

$$V = v_2 \frac{(C - c_2)}{(c_2 - c_1)} + v_1$$

where C = PEG concentration of test meal aliquot, v_2 = volume of test meal aliquot, c_1 = PEG concentration of gastric contents before adding test meal aliquot, c_2 = PEG concentration of gastric contents after adding test meal aliquot and v_1 = volume of sample of gastric contents withdrawn immediately before adding test meal aliquot. The amount of test meal remaining in the stomach is estimated using the volume calculated according to the equation above and the changes of the PEG concentration during the study.

After 50 to 100 min the procedure was finished by withdrawing the remaining gastric contents and washing out the stomach with 5 ml of saline. The total residue of the meal was calculated using the PEG concentrations of the recovered gastric contents and of the wash-out.

The gastric quarter-, half- and three-quarter-emptying times, i.e. the time required to empty 25, 50 and 75% of the test meal, respectively, were obtained by interpolation from individual emptying curves.

Analytical method. PEG was estimated turbidimetrically by the method of Hyden (10) using the modifications by Boulter & McMichael (1).

Test of validity. The validity of the marker dilution technique in estimating known amounts of test meals of infant formula was tested *in vitro*. A small amount of 0.1 molar hydrochloric acid was added to a vessel containing a known amount of infant formula and PEG. After mixing, the amount of infant formula in the vessel was estimated using the procedure described above. A part of the contents of the vessel was removed, another small amount of hydrochloric acid was added and the amount of infant formula remaining in the vessel was again estimated. The

Table 2. Data on infant formula

Energy content	2 900 kJ/l
Osmolality	290 mOsm/kg
<i>Composition</i>	
Protein	16
Casein	6.5
Whey proteins	9.5
Fat	35 ^a
Lactose	72
Sodium	0.2
Potassium	0.7
Calcium	0.4
Phosphorus	0.26

^a Fat is derived from lard, palm oil, cottonseed oil and sunflower oil. The amount of linoleic acid corresponds to 6% of the total energy content.

Table 3. Weighed versus experimentally estimated amounts of test meal in vitro

Estimation no.	Test meal (ml)		Difference (ml)
	Weighed	Estimated	
1	29.1	28.6	0.5
2	19.7	17.1	2.6
3	11.4	11.9	-0.5
4	7.6	7.1	0.5
5	4.3	3.9	0.4

procedure was repeated three more times. The amounts added to or removed from the vessel as well as the vessel including the test meal were weighed accurately. The results of this test are presented in Table 3.

Statistical methods. Student's *t*-test, linear regression analysis, and the Fisher exact probability test were used in the statistical analysis.

RESULTS

Emptying patterns. In 27 of the 30 studies gastric emptying had started at the first volume determination. A biphasic emptying pattern with an initial rapid phase lasting some 20 min followed by a slower phase was found in 19 of these 27 studies. The emptying rate appeared constant from the start in 5 studies including 4 performed with infant formula. In 3 studies (2 with human milk) only small amounts had emptied at the first determination. The subsequent emptying was faster.

In two of the three remaining studies, both with infant formula, no emptying had occurred at the first determination 16 and 21 min after feeding, respectively. Following this initial delay gastric emptying proceeded with a constant rate in one study while in the other study the emptying curve was biphasic with an initial rapid phase.

In the remaining study it was not possible to draw conclusions about the initial emptying as the first volume determination was invalidated by improper positioning of the feeding tube.

In 16 studies where meals of human milk and infant formula were given to the same infant the biphasic emptying pattern with an initial fast phase was observed significantly

more often than any of the other emptying patterns after meals of human milk than after meals of infant formula ($p = 0.024$).

The biphasic emptying pattern is illustrated in Fig. 1, which shows the gastric emptying in 4 studies performed in one infant.

Gastric emptying times. The gastric emptying times for one quarter, half and three quarters, respectively, of a test meal are presented individually in Table 4. The means and standard deviations of these emptying times are shown in Table 5.

The quarter-, half- and three-quarter-emptying times for meals of infant formula were significantly longer than for meals of human milk ($p < 0.001$).

No relationship was found between the time needed to administer the test meal and the gastric quarter- and half-emptying times.

Gastric emptying rate. Sixty minutes after administration of the meal 24.8 ± 7.5 ml of human milk meals and 19.2 ± 4.7 ml of infant formula meals had left the stomach. The difference is significant ($p < 0.05$).

The corresponding figures calculated per 0.1 m^2 of body surface area are 19.4 ± 4.5 ml and 13.8 ± 2.8 ml, respectively. The difference is significant ($p < 0.01$).

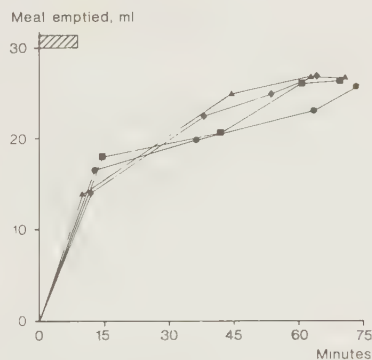


Fig. 1. Gastric emptying in a 5-week-old preterm infant (patient no. 6) after 30 ml test meals of human milk. The amount of meal that has left the stomach is plotted against time. Results are from four different studies performed on four consecutive days. The shaded area indicates the mean duration of the administration of the meals.

Table 4. Gastric emptying times in 11 healthy preterm infants

H = human milk, F = infant formula, lat = right lateral

Patient no.	Age at time of study (weeks)	Body weight at time of study (g)	Body position	Test meal (ml)	Time for injecting test meal (min)	Time in min for emptying of specified fraction of test meal		
						25%	50%	75%
1	5	1 380	Lat	30 H	12	8	16	52
			Lat	30 H	12	8	15	23
			Lat	30 H	12	8	32	52
2	2	1 780	Lat	40 F	4	22	50	95
3	2	1 820	Lat	40 F	6	28	49	74
4	2	1 900	Lat	60 H	6	16	32	66
			Lat	50 H	4	12	23	33
5	8	1 600	Lat	30 H	8	7	30	50
	9	1 780	Lat	35 H	10	5	12	26
			Lat	35 H	15	24	36	79
6	4	1 180	Lat	30 H	9	7	15	36
	5	1 270	Prone	30 H	9	5	16	39
			Prone	30 H	12	7	13	49
			Prone	30 H	10	6	12	59
			Prone	30 F	11	36	54	79
7	2	1 075	Lat	25 H	7	11	36	54
	3	1 180	Lat	25 H	8		44	62
			Lat	30 H	10	6	12	22
8	6	1 390	Prone	25 H	7	14	27	40
	7	1 500	Prone	25 H	15	20	30	60
			Prone	25 F	5	28	48	66
9	1	1 450	Lat	25 H	7	18	34	64
10	2	1 410	Prone	25 H	12	8	16	64
	3	1 510	Prone	30 H	16	35	52	78
			Lat	30 F	13	34	58	76
			Prone	40 F	11	27	60	97
11	2	1 420	Prone	25 H	8	8	17	48
	3	1 570	Lat	30 H	15	12	32	72
			Prone	30 F	11	53	64	79
	4	1 760	Prone	40 F	9	12	32	74

Gastric emptying rate and postconceptional age of the infant were not significantly correlated ($r=0.31$, $p>0.05$). The rate of emptying was, however, related to the infant's body surface area ($r=0.43$, $p<0.02$) and body weight ($r=0.40$, $p<0.05$).

DISCUSSION

Comparison of methods. Accurate data on gastric emptying of complete meals in the newborn and young infant are scarce. Earlier investigators have used radiological techniques in assessing gastric emptying of milk meals

containing barium in infants (16). Because of radiation hazards and poor correlation with more accurate methods (6) these techniques are, however, unsuitable.

Gastric emptying has been studied in infants using the serial test meal (9). This technique does not, however, allow one to follow the whole emptying course of a single meal. This is possible using radioisotope techniques (17). The methods involved are, however, intricate.

The marker dilution technique is simple and makes it possible to follow the gastric evacuation of a single and complete meal during the whole postprandial phase. The validity of the

Table 5. Gastric emptying of human milk and infant formula in preterm infants

Mean values $\pm$ S.D.

Test meal	Gastric emptying time (min) Percent of test meal emptied		
	25	50	75
Human milk	11.7 $\pm$ 7.5 (n=21)	25.1 $\pm$ 11.5 (n=22)	51.3 $\pm$ 16.7 (n=22)
Infant formula	30.0 $\pm$ 11.9 (n=8)	51.9 $\pm$ 9.8 (n=8)	80.0 $\pm$ 10.7 (n=8)

marker dilution technique is demonstrated by the *in vitro* test where calculated amounts agree closely with known amounts.

PEG has been used extensively as a volume indicator in studies of intestinal absorption and has also proved to be valid as a gastric non-absorbable indicator for studies in man (11).

Gastric emptying pattern. The biphasic emptying pattern which was found in most of the studies occurred significantly more frequently after meals of human milk than after meals of infant formula which usually were associated with a linear emptying pattern or with an initial delay of gastric emptying. The differences in emptying of the meals appear to be due to differences in the composition of human milk and infant formula.

Gastric emptying times. Gastric emptying times were short (Table 5). The differences in the emptying patterns between the two meals is reflected by the different gastric emptying times, which were significantly longer for meals of infant formula than for meals of human milk.

The half time of the meal in the stomach observed in the present study is considerably shorter than the figure reported by Signer & Fridrich (17) in infants given a standard meal of infant formula. This may at least in part be due to different meal volumes and different body positions being used in the two studies (19).

Gastric emptying rate. The average amount of meal that had left the stomach during the

first 60 min of a study was significantly larger for meals of human milk than for meals of infant formula. Keller (12) in a study on gastric emptying of human milk in infants found, that the gastric emptying rate was constant and proportional to the infant's body surface area corresponding to an emptying of 22 ml per 0.1 m² body surface area per hour. The emptying rate for meals of human milk found in the present study agrees fairly well with this figure.

Conclusion. The present study shows that healthy preterm infants, even if weighing slightly but above 1000 g, have a rapid gastric emptying after a feed of human milk. Gastric emptying times for meals of infant formula were roughly twice as long as those for meals of human milk.

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GASTRIC EMPTYING IN INFANTS FED HUMAN MILK OR
INFANT FORMULA

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Gastric emptying of meals of human milk or infant formula was studied in 17 healthy infants aged 4 weeks to 6 months using a marker dilution technique. In the 24 studies performed gastric emptying followed a biphasic pattern in 11 and a linear pattern in 12 studies. The average gastric half-emptying time for meals of human milk was 48 minutes, and for meals of infant formula 78 minutes. After 1 hour an average of 29.5 ml of human milk and 22.7 ml of infant formula per 0.1 m^2 of body surface area had emptied from the stomach.

Rapid gastric emptying of meals of mother's milk has been reported in preterm infants (1). Preterm infants, furthermore, empty meals of infant formula only half as fast as meals of human milk. Whether this pattern of gastric emptying is peculiar to the preterm infant or whether it also occurs in term infants is not known. This study was performed in order to estimate gastric emptying in healthy term infants given meals of human milk or infant formula.

MATERIAL

Seventeen infants aged 4 weeks to 6 months were studied. Their average body weight was 4.94 kg (range 3.45-7.29). They were growing at a normal rate at the time of the study. Their psychosomatic development was normal. Twelve of the infants were attending Baby Health Centres and the parents were asked to let their infants take part in the study. One infant was in hospital for radiological investigation of the urinary tract after a urinary tract infection. Four infants were being investigated for symptoms unrelated to the gastrointestinal tract and subsequently proved to be healthy. The studies were made after informed consent of the parents.

METHODS

Twenty-four studies were performed in the infants. Eight infants were given meals of human milk usually from their mothers. Five of them were studied 2 or 3 times within a time span less than a week. The remaining 3 infants who received human milk were studied once. Nine infants were given meals of infant formula (Tables 1 and 2). The volume of the test meals averaged 32 ml/kg body weight (range 23-42) corresponding to the volume of the

Table 1. *Data on infant formula (Milkotal^R, Findus)*

Energy content 2900 kJ per liter	
Osmolality 290 mOsm per kilogram	
Composition (grams per liter)	
Protein	16
Casein	6.5
Whey proteins	9.5
Fat	35 ^a
Lactose	72
Sodium	0.2
Potassium	0.7
Calcium	0.4
Phosphorus	0.26

^a Fat is derived from lard, palm oil, cottonseed oil and sunflower oil. The amount of linoleic acid corresponds to 6 % of the total energy content.

ordinary meal that the infants were receiving at the time of the study. Each of the 2 infants who were studied 3 times was given one meal that was 50 % larger than the ordinary meal of the infant.

Table 2. *Fatty acid content of infant formula*
Total fat content 35 g per liter.

Fatty acid	Per cent of total fat content
8:0 - 12:0	≤ 1
14:0	≤ 2
16:0	25 - 33
16:1	1 - 3
18:0	11 - 17
18:1	32 - 39
18:2	16 - 18
18:3	≤ 1
20:0	≤ 1
20:1	≤ 2
Higher	≤ 1

The meals were given by injection through a feeding tube introduced into the stomach through the nose. The injection lasted 5 to 10 min. The distance that the feeding tube was inserted was calculated using Kaijser's data on suitable length of stomach tube as related to the height of the infant (2). Gastric emptying was studied using a marker dilution technique with polyethylene

glycol (PEG, Macrogol 3000) as an inert marker (1). The technique involves repeated intragastric volume determinations during 1 1/2 to 2 1/2 hours following the administration of the meal. The first volume determination was performed soon after the infant had received the meal, i.e. 15 to 30 min after feeding had started. It was followed by another 2 to 4 volume determinations. During the study the infant was kept in the supine position.

Student's t-test, linear regression analysis, and the Fisher exact probability test were used in the statistical analysis. In the infants studied more than once individual averages of gastric half-emptying time and gastric emptying rate were calculated and used in the statistical analysis.

RESULTS

Gastric emptying pattern. In all the 24 studies gastric emptying had started at the first volume determination. A biphasic emptying pattern with an initial rapid phase lasting about 15 min followed by a slower phase was found in 11 of the 12 studies performed with human milk

in those infants, who were studied more than once (Fig. 1). In the remaining 12 studies comprising 3 performed with human milk and 9 with infant formula the emptying rate appeared constant during the whole study (Fig. 2). A biphasic emptying pattern occurred significantly more often after meals of human milk than after meals of infant formula ($p < 0.001$).

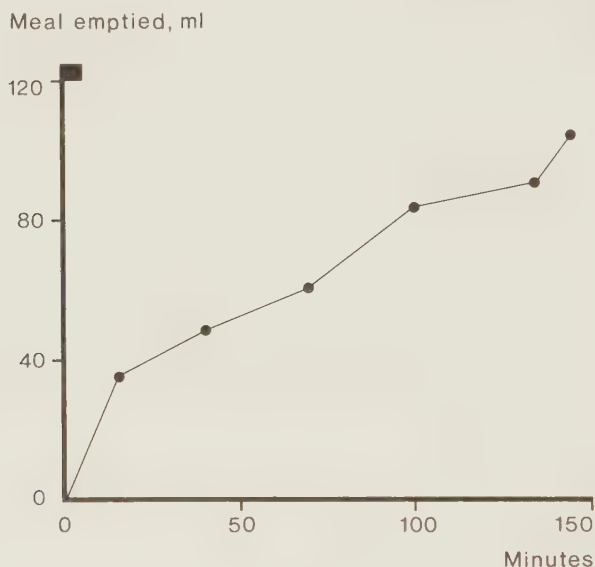


Fig. 1. Gastric emptying in a 4-week-old infant after a 120 ml meal of human milk. Black area indicates the duration of the administration of the meal.

Gastric half-emptying times. The gastric half-emptying times were 48 ± 15 min for meals of human milk and 78 ± 14 min for meals of infant formula. The difference be-

tween the half-emptying times is significant ($p < 0.01$).

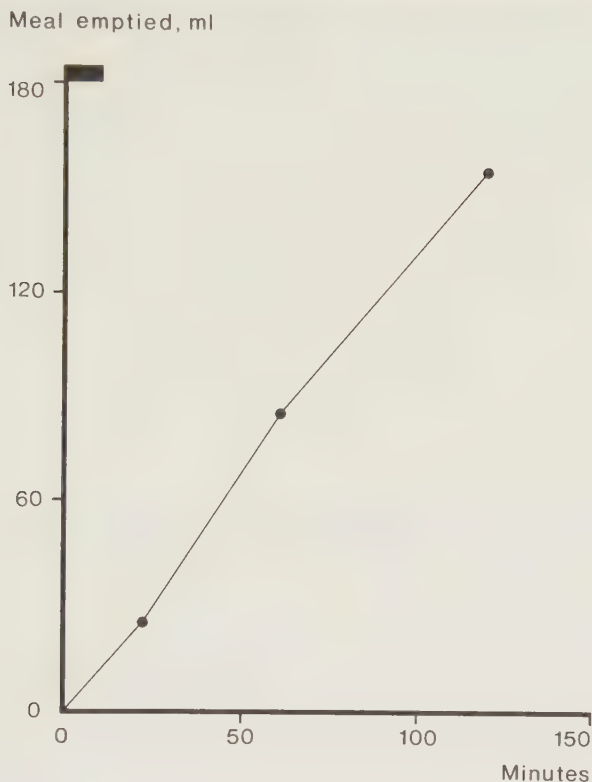


Fig. 2. Gastric emptying in a 9-week-old infant after a 180 ml meal of infant formula. Black area as in Fig. 1.

Gastric emptying rate. One hour after administration of the meal 29.5 ± 4.6 ml per 0.1 m^2 of body surface area of human milk meals had emptied from the stomach. The corresponding figure for infant formula meals was 22.7 ± 4.2 ml. The difference is significant ($p < 0.01$). After 2 hours 45.0 ± 4.9 ml of human milk meals and

39.3 $\pm$ 8.3 ml of infant formula meals per 0.1 m² of body surface area, respectively, had left the stomach. Gastric emptying rate calculated per body surface area unit and age of the infant were not significantly correlated (human milk meals, $r = -0.02$ and infant formula meals, $r = -0.18$).

DISCUSSION

In a study on gastric emptying in preterm infants emptying rate was greater and half-emptying times were shorter with meals of human milk than with meals of infant formula (1). Furthermore, a biphasic emptying pattern was observed more often after meals of human milk than after meals of infant formula. Similar differences in gastric emptying of meals of human milk and infant formula were found in the present study. Therefore, these differences do not seem to be related to the maturity of the infant.

Gastric emptying is influenced by the osmolality and composition of the meal emptying into the duodenum (3). Since human milk and the infant formula used in this study have equal osmolality and lactose concentration

the reason for the varying behaviour of the 2 meals may be their protein and fat components. The gastric half-emptying times for meals of infant formula agree fairly well with those reported by Signer & Fridrich (4) in infants given meals of infant formula. Gastric emptying rate for meals of human milk in the present study is greater than the figure reported by Keller (5) in a study on gastric emptying in infants. This may be due to different techniques being used in the two studies.

The rapid emptying of meals of human milk may partly explain the earlier return of pH of the gastric contents to pre-feed levels observed after these meals than found after meals of infant formula (6,7). A low pH in the infant's stomach may be important in preventing gastrointestinal infection (8). It remains to be studied whether the gastric emptying pattern with meals of infant formula can be modified by changing the composition of the formula including the quality of its constituents.

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GASTRIC EMPTYING IN INFANTS WITH CONGENITAL
HEART DISEASE

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Gastric emptying of infant formula using a marker dilution technique was studied in 8 infants with congenital heart disease aged one week to 5 months. Six infants were in heart failure and 4 failed to grow. Gastric emptying followed a linear pattern in 5 and a biphasic pattern with an initial slow phase in 2 infants. The amounts of meal emptied after 1 and 2 hours, 14.7 and 31.0 ml per 0.1 m^2 of body surface area, respectively, were significantly smaller than the corresponding amounts found in a group of healthy infants.

A small intake of feeding volumes is a common finding in infants with congenital heart disease (CHD) (1,2,3). Their decreased appetite has been ascribed to many factors. Reduced splanchnic blood flow and venous congestion of the gut have been suggested as important ones (4,5). Both are likely to alter the gastric emptying function and could therefore contribute to the anorexia that is observed in these infants. This study was performed in order to assess the gastric emptying function quantitatively in infants with severe CHD.

MATERIAL

Eight infants aged one week to 5 months with CHD were studied. They had been hospitalized for cardiac investigations and treatment. There were no extracardiac anomalies but one infant (No. 4) with TGA and VSD appeared dysplastic with hemifacial microsomia and low-set ears. On examination his chromosomes proved normal. He had an oxygen saturation in the systemic ventricle of 80 %. He had increased pulmonary blood flow and obvious signs of congestive heart failure. Congestive heart failure was present in 6 infants of the series and they were treated with digitalis. The remaining 2 infants had

slight cardiac symptoms and were therefore also treated with digitalis. All the infants except one (No. 3) were treated with diuretics as well but none was receiving oxygen therapy. The diagnosis was established by cardiac catheterisation in each patient. All the infants except one (No. 5) were unwilling or unable to consume sufficient food volumes and were therefore fed through a nasogastric infant feeding tube. All of them were fed infant formula. Three infants were 2 SD or more underweight as well as short relative to age according to Swedish growth standards (6). At the time of the study 4 of the infants (Nos. 2,4,5 and 8) were growing at a normal rate while 4 failed to grow. The clinical details of the infants are presented in Table 1. A group of 9 healthy infants aged 4 weeks to 6 months were used as controls. The infants were studied after informed consent of the parents and with approval of the Ethics Committee of the Medical Faculty, University of Lund.

Table 1. *Clinical data on infants with CHD*

Patient number	Age (weeks)	Diagnosis	Weight (SD) ^a	Length (SD) ^a	Respiratory frequency ^b	Duration of CHF (weeks)	P-Digoxin (nmol/l)	Tube feeding (weeks) ^c	Number of meals per day
1	6	VSD + PH	- 1.2	- 1	75	3	2.1	1	8
2	4	VSD + PH	0.5	0.5	70	4	2.9	4	6
3	1	TGA + VSD	- 0.5	- 0.5	70	1	3.9	1	6
4	17	CA	- 3	- 3	50	-	1.0	2	8
5	16	EF	- 1	- 0.5	55	-	1.6	-	5
6	8	VSD + PDA + PH	- 2.5	- 2.5	60	2	2.0	2	5
7	22	EF	- 1.5	- 2	60	4	1.7	3	5
8	16	VSD + PH	- 3	- 3	80	8	1.2	12	8

VSD = Ventricular septal defect, PH = Pulmonary hypertension (high pulmonary artery pressure and hyperkinetic pulmonary circulation), TGA = Transposition of the great arteries, CA = Coarctation of the aorta, EF = endocardial fibroelastosis, PDA = Patent ductus arteriosus, CHF = Congestive heart failure.

^a Weight and length expressed as multiples of standard deviations from the mean according to Swedish growth standards (6)

^b Respiratory frequency is expressed as the average respiratory rate per minute of the 24 hours preceding the gastric emptying study

^c Number of weeks that the patient had been fed by tube at the time of the study

METHODS

Test meals consisted of a commercial infant formula (Table 2) to which polyethylene glycol (PEG, Macrogol 3000) was added as an inert marker in a concentration

Table 2. *Data on infant formula*

Energy content 2900 kJ per liter	
Osmolality 290 mOsm per kilogram	
Composition (grams per liter)	
Protein	16
Casein	6.5
Whey proteins	9.5
Fat	35 ^a
Lactose	72
Sodium	0.2
Potassium	0.7
Calcium	0.4
Phosphorus	0.26

^a Fat is derived from lard, palm oil, cottonseed oil and sunflower oil. The amount of linoleic acid corresponds to 6 % of the total energy content.

of 0.25 % (w/v). The volumes of the meals corresponded to the volumes that the infants were receiving at regular meals at the time of the study and averaged 23 and 33 ml per kg for CHD and normal infants, respectively. The meals were administered through a naso-gastric tube after the gastric contents had been withdrawn and the stomach washed out with saline. The injection rate was adapted to the infant's condition and the injection generally lasted 10 to 20 minutes.

Gastric emptying was estimated using a marker-dilution technique (7). Specified amounts of PEG dissolved in an aliquot of the test meal were introduced into the stomach and mixed with the gastric contents at various intervals after administration of the meal. By analysing the dilution of PEG in the gastric contents the amount of meal remaining in the stomach was calculated. Two or 3 determinations were made, the first one about 10 min after the meal had been given, the second and third ones 1 and 1 1/2 hour, respectively, after starting the procedure which was finished after 2 hours by withdrawing the gastric contents and washing out the stomach with saline. The remainder of the meal was calculated from the PEG recovered from the withdrawn contents and the wash-out. Individual emptying curves were plotted and the gastric half-emptying times and the amounts of meal emptied from the stomach after 1 and 2 hours, respectively, were obtained by interpolation.

Analytical method. PEG was estimated turbidimetrically by the method of Hydén (8) using the modifications by Boulter & McMichael (9).

Statistical methods. Standard statistical methods were used. Data in the text are given as mean $\pm$ SD.

RESULTS

Gastric emptying pattern. In 7 of the 8 patients with CHD gastric emptying had started at the time of the first determination of the amounts of meal in the stomach, i.e. about 10 minutes after the meal had been given. Following this, gastric emptying proceeded at the same rate as before in 5 infants and at a faster rate in 2 infants (Nos. 3 and 7). In another infant (No. 5) no significant emptying of the meal had occurred after 1 hour, but then the stomach started emptying at a constant rate. Gastric emptying followed a linear pattern in all the infants of the control group.

Gastric emptying times. Gastric half-emptying times of infants with CHD are presented individually in Table 3. The mean gastric half-emptying time (68 ± 17 minutes) does not differ significantly ($p > 0.05$) from the corresponding figure (78 ± 14 minutes) found in the control group (Table 4).

Table 3. *Gastric emptying in infants with CHD*

Patient number	Gastric half-emptying time (min)	Amount of meal emptied from the stomach after specified time (ml per 0.1 m ² of body surface area)	
		1 hour	2 hours
1	60	16.8	31.6
2	44	22.6	34.4
3	67	13.5	29.7
4	61	15.9	27.8
5	103	0	34.2
6	66	15.9	30.4
7	73	17.6	31.8
8	66	15.3	28.6
Mean $\pm$ SD	68 $\pm$ 17	14.7 $\pm$ 6.5	31.0 $\pm$ 2.4

Gastric emptying rate. The amounts of meal per 0.1 m² of body surface area emptied from the stomach after 1 and 2 hours, respectively, in the infants with CHD are presented in Table 3. These amounts are significantly smaller ($p < 0.01$ and $p < 0.05$, respectively) than those of the infants in the control group, which are presented in Table 4. The amounts of meal leaving the stomach during the second hour did not differ significantly ($p > 0.05$) between the two groups of infants.

Gastric emptying rate was not significantly correlated

Table 4. Gastric emptying in healthy infants

Subject number	Age (weeks)	Gastric half-emptying time (min)	Amount of meal emptied from the stomach after specified time (ml per 0.1 m ² of body surface area)	
			1 hour	2 hours
1	24	101	20.4	31.1
2	9	67	30.9	57.7
3	8	75	21.0	38.7
4	4	79	20.2	36.7
5	24	84	23.3	37.1
6	9	55	26.9	43.3
7	8	67	23.6	40.3
8	13	87	16.3	28.8
9	21	84	22.0	40.2
Mean ± SD		78 ± 14	22.7 ± 4.2	39.3 ± 8.3

with the age of the patients ($r = -0.25$, $p > 0.05$) or of the controls ($r = -0.18$, $p > 0.05$).

DISCUSSION

Gastrointestinal hypomotility with delayed gastric emptying has been reported to occur in congestive heart failure (10) and hypoxia has been shown to delay gastric emptying time in man (11). All the infants with CHD in the present study were seriously ill, 6 of them having

obvious signs of heart failure. One patient (No. 3) had cyanotic heart disease. He was included in the series because of apparent signs of heart failure. Considering the severity of their heart disease these infants would be expected to show abnormalities in gastric function.

Gastric function was estimated using the average gastric emptying rate during the first and second hour, respectively, after administration of a test meal. During the first hour gastric emptying was significantly slower in infants with CHD than in age-matched healthy infants of a control group. During the second hour, however, gastric emptying rate did not differ significantly between the two groups.

These findings are consistent with the differences in emptying pattern between the two groups that were found. Three of the eight infants with CHD showed a biphasical emptying pattern with an initial slow phase, while all the infants in the control group showed a linear pattern. There were no clinically distinctive marks in the infants with a biphasical emptying pattern.

Differences in emptying pattern alone, can, however, hardly explain the differences in average gastric emp-

tying rates of the two groups, as the remaining 5 infants with CHD, who displayed a linear emptying pattern, also proved to empty their stomachs slower during the first hour than did the infants in the control group.

Gastric emptying rate as influenced by the volume of the meal that is put into the stomach, i.e. the larger the meal the higher the emptying rate (13,14). The rather small meal volumes received by the infants with CHD may therefore have contributed to their slow emptying rates during the first hour after administration of the meal. Gastric emptying rate in the two groups did not differ during the second hour although the infants in the CHD group had significantly smaller amounts of meal remaining in their stomachs than the controls. This is probably because during the second hour, the driving effect of the decreasing volume of the gastric contents has levelled off.

Gastric hypomotility, as a consequence of splanchnic congestion or hypoperfusion, may also have contributed to the rather slow gastric emptying during the first hour in the infants with CHD, considering the severity of their clinical condition.

Sondheimer & Hamilton (12) found only mild abnormalities in digestive tract function unrelated to the severity of the cardiac lesion in infants with CHD, including several ones with congestive heart failure, and they suggested that the gut normally has a large circulatory reserve. Their study focused, however, on the absorptive capacity of the gut, and therefore, does not exclude abnormalities in the motor function of the gastrointestinal tract in infants with severe CHD.

The present study suggests that infants with CHD have a reduced capacity for emptying a meal of standard infant formula from their stomachs. It has been suggested that these infants should be given meals with raised energy density in order to get an adequate nutritional supply (1). Further studies are needed to assess their capacity for emptying meals with increased energy concentration.

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EFFECT OF FEEDING AN INFANT FORMULA WITH HIGH ENERGY
DENSITY ON GASTRIC EMPTYING IN INFANTS WITH CONGENITAL
HEART DISEASE

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Gastric emptying of meals of standard infant formula and formula fortified with a glucose polymer (Caloreen) were compared in 7 infants with severe congenital heart disease aged 9 days to 5 months. A marker dilution technique was used in estimating gastric emptying. Gastric half-emptying times were significantly longer

Part of this work was presented at the 13th Annual Meeting of the European Society for Pediatric Gastroenterology and Nutrition in Capri, May 27-29, 1980 (1).

for meals containing Caloreen than for meals of standard infant formula. Although significantly smaller amount of meal containing Caloreen had left the stomach after 2 hours, the net transfer of energy to the intestine was larger than after feeding a standard meal.

The voluntary intake of food of the infant with severe congenital heart disease (CHD) is often poor as compared with that of healthy infants of similar size. Furthermore, energy requirements per unit of body-weight are greater than for normal individuals (2). In order to provide an adequate nutritional supply to infants with CHD feeding of small volumes of formula with a high energy density have been suggested (2,3,4). Increasing the energy density of a meal slows gastric emptying (5). A further decrease of the already lowered gastric emptying rate in infants with severe CHD (6) would, however, be undesirable considering their breathlessness and feeding difficulties.

The purpose of this work was to study the effect of raising the energy density of a meal by adding a glucose polymer on gastric emptying in infants with severe CHD.

CLINICAL MATERIAL AND METHODS

Seven patients who were in hospital for investigation of CHD took part in this study. The clinical data on the patients have been presented in a previous paper (6).

Each infant received 2 test meals of a standard formula containing 0.25 % polyethylene glycol (PEG, Macrogol 3000) as an inert marker. A glucose polymer (Caloreen) was added to one of the meals. Four infants had meals containing 4 % and the remaining infants had meals containing 7.5 % of Caloreen. The addition of 4 and 7.5 % of Caloreen to the formulas increased the energy density from 2900 kJ per liter to 3570 and 4200 kJ per liter, respectively.

The meals were injected into the stomach via a feeding tube and gastric emptying of the meals was studied using a marker-dilution technique (7).

Statistical methods. Statistical analysis was carried out using a t-test for paired comparisons between the two test meals. A one-sided test was used for evaluating differences in gastric half-emptying time and in gastric emptying of amounts of meal. Differences in gastric emptying of amounts of energy contained in the meals were tested using a two-sided test.

RESULTS

Gastric emptying pattern. In 6 infants an almost identical emptying pattern was found in the two studies which were performed in each patient. Four of these infants showed a linear emptying pattern with a constant emptying rate during the whole emptying period, while 1 infant displayed a biphasic emptying pattern with an initial slow phase lasting about 20 minutes followed by a faster linear phase. In one patient gastric emptying had not started until one hour after the meal of standard infant formula had been given. Gastric emptying then proceeded rapidly with a constant rate. After the meal containing Caloreen an almost identical emptying pattern was found. During the first half hour only about 7 % of the meal had left the stomach. After an interval lasting one hour during which no emptying occurred a phase with a rapid emptying rate followed.

In the remaining infant gastric emptying of standard infant formula followed a linear pattern, whereas the meal of formula containing Caloreen was emptied with a biphasic pattern with an initial slow phase followed by a rapid phase.

Gastric half-emptying times. The average gastric half-emptying time for meals of standard infant formula was 67 ± 18 minutes. The corresponding figure for meals containing Caloreen was 79 ± 19 minutes. The addition of Caloreen to the meals prolonged the half-emptying times significantly ($p < 0.05$).

Gastric emptying rate. The amounts of meal per 0.1 m^2 of body surface that had left the stomach after 1 and 2 hours, respectively, are presented individually in Table 1. The corresponding amounts of energy are pre-

Table 1. Gastric emptying of infant formula without and with Caloreen in infants with CHD

Patient number	Amount of meal emptied (ml per 0.1 m^2 of body surface area)			
	Infant formula		Infant formula with Caloreen	
	1 hour	2 hours	1 hour	2 hours
1	16.8	31.6	13.6	30.4
2	22.6	34.4	8.4	28.1
3	13.5	29.7	9.1	22.9
4	15.9	27.8	13.7	25.9
5	0	34.2	2.9	29.5
6	15.9	30.4	18.3	29.2
7	15.3	28.6	13.8	23.1
Mean $\pm$ SD	14.3 $\pm$ 6.9	31.0 $\pm$ 2.6	11.4 $\pm$ 5.0	27.0 $\pm$ 3.1

sented in Table 2. Neither the amounts of meal nor the amounts of energy that emptied from the stomach during the first hour after administration of the meal differed significantly. In contrast, significantly larger volumes of standard infant formula had left the stomach after 2 hours compared with meals containing Caloreen ($p < 0.005$). The corresponding amounts of energy that had passed the pylorus was, however, significantly larger for the meals with high energy density ($p < 0.02$).

Table 2. Gastric emptying of energy with a meal in infants with CHD given meals of infant formula without and with Caloreen

Patient number	Amount of energy emptied (kJ per 0.1 m^2 of body surface area)			
	Infant formula		Infant formula with Caloreen	
	1 hour	2 hours	1 hour	2 hours
1	48.7	91.6	57.1	127.7
2	65.5	99.8	35.3	118.0
3	39.2	86.1	38.2	96.2
4	46.1	80.6	48.9	92.5
5	0	99.2	10.4	105.3
6	46.1	88.2	65.3	104.2
7	44.4	82.9	49.3	82.5
Mean $\pm$ SD	41.4 $\pm$ 20.0	89.8 $\pm$ 7.5	43.5 $\pm$ 17.9	103.8 $\pm$ 15.4

All meals were well tolerated by the infants but one

individual had transient loose stools the day after having had a meal containing 7.5 % of Caloreen.

DISCUSSION

The difficulties in consuming sufficient volume of feed by infants with severe congenital heart disease often result in a subnormal intake of energy, contributing to the growth failure usually seen in these infants (2,8,9). By feeding frequent small volumes enriched with carbohydrate or fat weight gain could, however, be induced in infants with CHD (2).

Slowing of the gastric emptying rate as a result of an increase of the energy density of a meal has been reported in healthy neonates and in infants given meals of varying glucose concentrations (10,11). There are no previous data on gastric emptying of fortified complete meals in infants with CHD.

In the present study the slowing effect on gastric emptying of adding Caloreen was clearly demonstrated by the significantly smaller amounts of meal containing Caloreen that had left the stomach after 2 hours com-

pared with meals of standard infant formula. The transfer of energy to the intestine during the same time was nevertheless significantly larger with meals containing Caloreen, the slowing effect on gastric emptying of the added glucose polymer being insufficient to offset the raised energy density of the meal. An increase in the delivery of energy to the duodenum with meals of high nutritive density simultaneously with a reduced gastric emptying rate has been reported in adults (5). Husband and Husband (10) found in the newborn that, although 10 % glucose emptied at a slower rate than 5 % glucose, more glucose left the stomach in a given time when the more concentrated solution was given, and they concluded that for intermittent feeding, 10 % glucose is preferable to 5 % glucose when a high energy intake is desired.

Adding Caloreen to the meals did not seem to influence gastric emptying patterns appreciably, an almost identical pattern being found in the two studies in 6 out of 7 infants. This suggests that the shape of the individual emptying curve - as far as the effect of the meal is concerned - is mainly determined by the composition of the standard infant formula.

Although being significant, the difference between the

amounts of meal emptied after 2 hours was only 4.0 ml per 0.1 m^2 of body surface area. Such a small difference of volume is unlikely to put an increased stress even on the infant with severe CHD. Furthermore, none of the infants showed clinical evidence of being more distressed after fortified meals than after meals of standard infant formula.

The consuming of a meal containing 7.5 % of Caloreen, i.e. a total carbohydrate concentration of 15 %, may have contributed to the loose stools which were observed in one infant. Although most infants tolerate between 10 and 12 grams of carbohydrate per 100 ml and some infants even 15 to 20 grams of carbohydrate per 100 ml (12), there is obviously a risk of diarrhoea with a carbohydrate concentration of this magnitude.

A moderate increase in carbohydrate concentration of a standard infant formula, e.g. by adding 4 % of Caloreen, will provide a valuable contribution of energy to the infant with severe CHD without reducing gastric emptying rate to an extent that would put a strain on the patient. Further studies are needed to evaluate the effect on weight gain of a formula with high energy density in infants with CHD.

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GASTRIC EMPTYING IN INFANTS WITH CYSTIC FIBROSIS

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Gastric emptying of meals of pasteurized human milk or infant formula was studied in 4 infants aged 5 weeks to 4 months with cystic fibrosis (CF) and pancreatic insufficiency. A marker dilution technique was used. Three of the patients showed gastric emptying rates higher than those of controls during the first hour after receiving the meal. The gastric emptying rate of the remaining patient, both after a meal of human milk and of infant formula, was similar to that of the controls.

Rapid gastric emptying of liquid meals containing protein, fat and carbohydrate has been reported in adult patients with pancreatic insufficiency (1,2). The failure of the patients to retard gastric emptying has been ascribed to an inadequate intraluminal digestion, particularly of fat (1,2,3). A majority of patients with cystic fibrosis (CF) have a completely absent pancreatic exocrine secretion from birth leading to malabsorption, especially of fat and protein. In view of this gastric emptying was assessed during early life in infants with CF and pancreatic insufficiency.

MATERIAL

Four infants aged 5 weeks to 4 months with CF were studied. The diagnosis was based on the clinical symptoms and the finding of abnormally high sweat electrolyte levels. The clinical and laboratory data on the patients are presented in Table 1. They were all breast-fed except patient LR, who received infant formula. The pancreatic function of the patients was clearly abnormal as evidenced by the low enzyme activities in their duodenal contents and by their abnormal fat absorption. None of the patients had pulmonary symptoms.

Table 1. *Clinical and laboratory data on patients with CF*
 FG = Failure to grow

Patient	Age (weeks)	Weight (kg)	Sweat test (Na mmol/l)	Fat absorption (per cent)		Pancreatic function Enzyme activities in duodenal contents ^a (μ mol/min/ml)		Previous history
				Human milk	Infant formula	Chymo- trypsin	Lipase	
AL	7	3.8	90	67		2.2	12.5	Meconium ileus, FG, Steatorrhoea
CP	16	5.1	76	18		2.0	1.0	FG neonatally, Steatorrhoea,
LR	5	3.5	55		19	1.0	9.2	Positive meconium albumin test, FG, Steatorrhoea
JL ^b	18	4.0	86	76		4.8	32.8	Positive meconium albumin test, FG

^a Enzyme activity expressed as maximal level attained during any collection period following a test meal

^b Patient JL received fresh mother's milk at the fat absorption and pancreatic function studies.

METHODS

Studies on gastric emptying, pancreatic function and fat absorption were done in each patient with a time span of 8 weeks or less.

General procedure

The patients were given test meals of pooled pasteurized human milk or of a commercial infant formula (Table 2).

Table 2. *Data on infant formula*

Energy content 2900 kJ per liter	
Osmolality 290 mOsm per kilogram	

Composition (grams per liter)	
Protein	16
Casein	6.5
Whey proteins	9.5
Fat	35 ^a
Lactose	72
Sodium	0.2
Potassium	0.7
Calcium	0.4
Phosphorus	0.26

^a Fat is derived from lard, palm oil, cottonseed oil and sunflower oil. The amount of linoleic acid corresponds to 6 % of the total energy content.

Two patients (LR and JL) received meals both of human

milk and of infant formula on separate occasions. Polyethylene glycol (PEG, Macrogol 3000) was added to the meals as an inert marker in a concentration of 0.25 % (w/v). The volume of the meals averaged 153 ml corresponding to the volume of the patients' ordinary meals. The meals were given via a nasogastric feeding tube. Seventeen healthy age-matched infants, 8 of which received human milk and 9 of which received infant formula, were used as controls. The studies were performed after informed consent of the parents.

Gastric emptying of the test meal

A marker dilution technique was used in estimating gastric emptying of the test meal (4). Two or three determinations were made, the first one about 10 minutes after administration of the meal. The second and third determinations of meal volume were made about 1 and 1 1/2 hour, respectively, after starting the procedure, which was finished after 1 and 1 1/2 to 2 hours by withdrawing the gastric contents and washing out the stomach with saline.

The amounts of meal emptied after 1 hour were obtained by interpolation from the individual emptying curves.

Assessment of pancreatic function

Fasting samples of duodenal contents were aspirated by siphonage and collected in ice cooled tubes for 30 minutes. Serial samples were collected in the same way during 6 subsequent 10-minute periods followed by two 30-minute periods after the patient had received a meal of pasteurized human milk or of infant formula. Patient JL was given a meal of fresh mother's milk. The samples were frozen and later analysed for chymotrypsin and lipase.

The sweat test

Sodium concentration was estimated in sweat collected after pilocarpine iontophoresis (5).

Test of albumin in meconium was done using the BMC strip test (6).

Fat absorption was assessed using 72-hour fat balance studies, the patients receiving fresh or pasteurized human milk. One patient was given infant formula during the balance study.

Analytical methods

PEG was estimated by the method of Hyđén (7) using the

modifications by Boulter & McMichael (8). Chymotrypsin was determined using the method of Haverback et al. (9). Enzyme activities were compared with concentrations of chymotrypsin in intestinal contents of healthy infants reported by Norman et al. (10), using 5.34 as a conversion factor to recalculate enzyme activities expressed as $\mu\text{mol}/\text{min}/\text{ml}$ (11). Lipase was estimated according to Erlanson & Borgström (12), and the results were compared with lipase activities in duodenal contents of healthy infants found by Fredrikzon & Bläckberg (13). Fecal fat was measured using the method of van de Kamer (14).

RESULTS

The gastric emptying rates of the patients, expressed as the amounts of meal per 0.1 m^2 of body surface area that left the stomach during the first hour after administration of the meal, are compared with those of the controls in Fig. 1. With the exception of patient JL, gastric emptying was faster in the patients with CF than in the controls, regardless of the quality of the meal. This was most obvious with meals of infant formula, where gastric emptying rates almost twice as great as those of the controls were found.

Meal emptied, ml/0.1 m² surface area

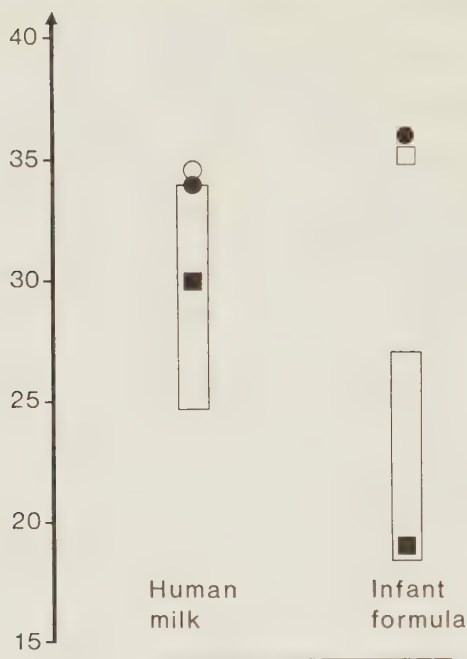


Fig. 1. Gastric emptying in infants with CF. The amount of meal per 0.1 m² of body surface area that has left the stomach 1 hour after administration of the meal is plotted for individuals. (O) = patient AL, (□) = patient CP, (●) = patient LR and (■) = patient JL. Columns represent amount of test meal emptied in the controls (mean $\pm$ 1 SD).

Patients JL and LR received meals both of pasteurized human milk and of infant formula. Patient JL emptied the two meals at rates similar to those of the controls, the emptying rate of the meal of human milk clearly exceeding that of the meal of infant formula. Patient LR emptied the two meals at a similar speed. Both meals were emptied faster than the meals received by the controls.

DISCUSSION

The exocrine pancreatic secretion of the patients in this study was abnormally low, and they all had fat malabsorption of varying degree. There was also clinical or laboratory evidence of protein maldigestion, one patient presenting with meconium ileus and two patients having a positive meconium albumin test. Patient LR had a sweat sodium concentration below 60 mmol per liter, but the diagnosis was accepted on clinical grounds and the observation of viscous duodenal secretions.

Gastric emptying is slowed by duodenal receptors sensitive to fat, osmolality and pH (15). Fat is a potent inhibitor of gastric emptying (15) but seems to require

digestion to exert its inhibiting effect (1,2,3). The slowing of gastric emptying by proteins in meals is assumed to be mediated by duodenal osmoreceptors stimulated by the products of hydrolysis (16).

The rapid gastric emptying which was observed in three of the patients can be explained by assuming an insufficient intraluminal digestion of the meal causing an inefficient feedback inhibition of the stomach. There are no reports on gastric emptying in infants with CF, but rapid gastric emptying of fatty meals has been found in adults with chronic pancreatitis and steatorrhoea (2, 3). By adding pancreatic enzymes to the meals it was possible to slow gastric emptying in patients with pancreatic insufficiency, which is consistent with the idea that an improved digestion of fat and protein contributed to the inhibition of gastric emptying (2). Roulet et al. (17) found, however, no difference in gastric emptying time between CF teenagers with pancreatic insufficiency and healthy controls. Differences in age of the patients and the composition of their meals, containing no protein, make comparison between their study and the present one difficult.

Patient JL emptied the meal of human milk as well as

that of infant formula at the same rate as the controls. Steatorrhoea appears only in severe pancreatic insufficiency in adults when most of the pancreatic enzyme secretion is lost (18). It is, however, not clear whether aberrations in gastric emptying appear only with severe enzyme deficiency (2). In patients with various malabsorptive states Moberg & Carlberger (1) found that the larger the steatorrhoea the larger the deviation from the normal gastric emptying pattern. The action of bile salt stimulated lipase in human milk (19) may have contributed to the relatively high percentage fat absorption found in patient JL. However, unlike the other patients, two of which also were breastfed, patient JL had no clinically overt steatorrhoea. Furthermore, she had higher chymotrypsin activities in duodenal contents than the other patients. This might explain why the gastric emptying rates of this patient were similar to those of the controls.

It has been proposed that rapid gastric evacuation overwhelming limited pancreatic reserves may contribute to maldigestion (2). This is an important aspect of the digestion of the infant with CF who fails to grow, and therefore further studies are needed to evaluate the effect of pancreatic substitution or of drugs on gastric emptying in these patients.

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TABLES

Table 1. *Gastric emptying in healthy infants*
A. Human milk

Subject No.	Age (weeks)	Weight (kg)	Length (cm)	Surface area (m ²)	Test meal (ml)	Emptying pattern	Half-emptying time (min)	Amount of meal emptied (ml/0.1 m ² surface area)	
								1 hour	2 hours
1	5	3.80	53	0.24	120	b	30	35.0	-
					120	b	20	31.7	42.5
2	4	3.48	51	0.23	90	b	45	23.6	37.3
					120	b	68	25.1	39.5
3	8	3.60	56	0.24	130	b	35	32.5	51.3
					130	e	52	28.6	41.2
4	4	3.45	52	0.23	80	b	28	27.6	-
					80	b	37	19.5	-
					120	b	25	37.6	44.7
5	8	4.60	57	0.27	130	b	62	25.3	-
					130	b	55	26.3	-
					195	b	83	29.7	46.5
6	8	5.12	59	0.29	160	1	48	36.1	54.0
7	13	5.16	59	0.30	160	1	68	23.1	41.9
8	13	5.83	64	0.33	180	1	51	33.1	50.2

B. Infant formula

Subject No.	Age (weeks)	Weight (kg)	Length (cm)	Surface area (m ²)	Test meal (ml)	Emptying pattern	Half-emptying time (min)	Amount of meal emptied (ml/0.1 m ² surface area)	
								1 hour	2 hours
1	24	7.29	69	0.38	225	1	101	20.4	33.8
2	9	4.40	56	0.27	180	1	67	30.9	57.7
3	8	4.98	56	0.28	150	1	75	21.0	38.7
4	4	4.30	54	0.26	150	1	83	21.0	42.3
5	24	5.97	62	0.33	220	1	84	23.3	37.1
6	9	5.49	59	0.31	150	1	82	26.9	43.3
7	8	4.67	59	0.28	150	1	67	23.6	40.3
8	13	5.90	60	0.32	150	1	87	16.3	28.8
9	21	5.92	64	0.33	220	1	84	22.0	40.2

b = biphasic; e = exponential; 1 = linear.

Table 2. Gastric emptying in preterm infants

Patient No.	Age (weeks)	Weight (g)	Length (cm)	Surface area (m ²)	Test meal (ml)	Emptying pattern	Amount of meal emptied (ml/0.1 m ² surface area/hour)
1	5	1380	40	0.125	30 H	b	20.8
					30 H	b	21.6
					30 H	b	19.8
2	2	1780	41.5	0.146	40 F	1	15.9
3	2	1820	42	0.149	40 F	1	15.1
4	2	1900	45	0.154	60 H	b	27.6
					50 H	b	30.5
5	8	1600	41.5	0.137	30 H	b	18.6
					35 H	b ₁)	20.9
					35 H	b ₁)	15.5
6	4	1180	38	0.112	30 H	b	22.5
5		1270	38.5	0.117	30 H	b	22.6
					30 H	b	22.1
					30 H	b	19.0
					30 F	s	13.6
7	2	1075	37.5	0.106	25 H	b	20.8
					25 H	-	17.2
					30 H	b	23.6
8	6	1390	39	0.125	25 H	1	20.0
7		1500	40	0.130	25 H	b	14.5
					0.133	1	12.6
9	1	1450	41.5	0.130	25 H	b	13.5
10	2	1410	39.5	0.125	25 H	b ₁)	14.4
					30 H	b ₁)	12.6
					30 F	b ₁)	11.8
					40 F	1	14.0
11	2	1420	40.5	0.127	25 H	b	14.4
					30 H	b	16.1
3		1570	41.0	0.135	30 F	s	18.9
4		1760	41.5	0.144	40 F	b	18.3

1) Initial slow phase.

H = Human milk; F = Infant formula; b = biphasic; 1 = linear; s = No emptying at first volume determination.

Table 3. Gastric emptying in infants with congenital heart disease

Patient No.	Age (weeks)	Weight (kg)	Length (cm)	Surface area (m ²)	Test meal (ml)	Emptying pattern	Amount of meal emptied (ml/ 0.1 m ² surface area)	
							1 hr	2 hrs
1	6	3.60	54	0.24	80 F 80 C	1 1	16.8 13.6	31.6 30.4
2	4	4.24	56	0.26	90 F 90 C	1 b	22.6 8.4	34.4 28.1
3	1	3.30	51	0.22	70 F 70 C	b b	13.5 9.1	29.7 22.9
4	17	3.85	55	0.25	80 F 80 C	1 1	15.9 13.7	27.8 25.9
5	16	5.57	62	0.31	150 F 150 C	1 ¹⁾ b	0 2.9	34.2 29.5
6	8	3.40	52	0.22	80 F 80 C	1 1	15.9 18.3	30.4 29.2
7	22	5.80	61	0.32	150 F	b	17.6	31.8
8	16	3.57	55	0.24	80 F 80 C	1 1	15.3 13.8	28.6 23.1

1) Linear emptying pattern after 1 hour.

F = Infant formula; C = Infant formula with Caloreen; b = biphasic; 1 = linear.

Table 4. *Gastric emptying in infants with cystic fibrosis*

Patient	Age (weeks)	Weight (kg)	Length (cm)	Surface area (m ²)	Test meal (ml)	Emptying pattern	Half- emptying time (min)	Amount of meal emptied (ml/0.1 m ² surface area)	
								1 hr	1.5 hr 2 hrs
AL	7	3.84	56	0.25	150 H	1	52	34.0	54.1
CP	16	5.10	59	0.29	154 F	1	40	35.2	48.7
LR	5	3.50	55	0.23	150 F	b	53	36.0	34.8
	10	4.32	59	0.27	175 H	1	58	34.2	60.2
JL	18	4.03	54	0.25	140 H	b	58	30.0	49.2
	19				150 F	1	94	19.0	45.1

H = Human milk; F = Infant formula; b = biphasic; 1 = linear.

